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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,351	01/26/2005	Bruce J. Simon	5490E-292/NPB	6317

7590 07/08/2009

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
07/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,351	SIMON, BRUCE J.	
	Examiner	Art Unit	
	SUSAN E. FERNANDEZ	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2009 and 11 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-9,12-15,17 and 19* is/are pending in the application.

4a) Of the above claim(s) *6-8,13 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,9,12,14,15 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 1, 2009, has been entered.

The amendment filed June 11, 2009, has been received and entered.

Claims 2, 4, 10, 11, 16, and 18 are cancelled.

Claims 1, 3, 5-9, 12-15, 17, and 19 are pending. Claims 6-8, 13, and 17 are withdrawn.

Claims 1, 3, 5, 9, 12, 14, 15, and 19 are examined on the merits to the extent they read on the elected subject matter and species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 15, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 15 now recite "inducing cell proliferation of endothelial cells" and claim 1 now recites "enhancing said bone or cartilage tissue defect," which are considered new matter. First, though the specification teaches inducing cell proliferation (page 4, line 32), the specification does not indicate that proliferation is induced of endothelial cells, specifically. Furthermore, the specification teaches the "repair or enhancement of tissue" and enhanced growth of blood vessels (page 5, lines 1 and 2). However, the specification does not teach that a bone or cartilage tissue defect is enhanced. It appears that the enhancement of a tissue detect would be opposite of the effect sought, which is the treatment of the tissue defect. Because the specification as filed fails to provide clear support for the new claim language, a new matter rejection is clearly proper.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 12, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered indefinite by the recitation "enhancing said bone or cartilage tissue defect." It is unclear what is meant by the enhancement of a tissue defect. Thus, claims 1, 3, and 5 are rejected under 35 U.S.C. 112, second paragraph.

Regarding claim 12, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 15 is rendered indefinite by the recitation "enhance said tissue." It is unclear what characteristic of the tissue is enhanced. Moreover, "said tissue" lacks antecedent basis. Thus, claims 15 and 19 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5, 9, 12, 14, 15, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton et al. (US 6,372,494) in view of Baylink (US 5,195,940) and/or George et al. (US 6,334,069), and further in view of Yen-Patton et al. (Journal of Cellular Physiology. 1988. 134: 37-46).

Naughton et al. discloses conditioned cell medium compositions which are conditioned using any eukaryotic cell type (abstract). A culture medium is incubated with cells in order to obtain a "conditioned cell medium" (column 1, lines 30-32). The culture medium may be conditioned by stromal cells preferably in a three dimensional tissue construct (column 4, lines 49-53), which can be further cultured with parenchymal cells (column 5, lines 4-8). The stromal cells that can be cultured can include endothelial cells (column 12, lines 46-49), as required by instant claims 2, 10, and 18.

Additionally, "the cells can be cultured by any means known in the art" (column 19, line 62) and once the culture medium is conditioned so that the extracellular proteins such as growth factors have reached desirable levels in the media, the conditioned medium is pumped out of the culturing system and processed for use (column 20, lines 15-19). It is noted in Naughton et al. that "…the conditioned media provided by the present invention is also useful in the treatment of other types of tissue damage, e.g. traumatic or congenital, wherein the repair and/or regeneration of tissue defects or damage is desired since many of these growth factors are found in Applicants' conditioned cell media…" (column 22, lines 4-9). For instance, the conditioned medium of Naughton et al. may be used in the treatment of broken bones (column 22, lines 27-31) and cartilage (column 25, lines 13 and 14). Therefore, limitations recited in instant claims 4, 5, and 14 (culture medium for treatment of bone tissue defects wherein broken bone is a defect associated with osteoporosis, spinal fixation procedure, joint replacement procedure, bone fracture; growth factors present in culture medium) are taught by Naughton et al. Moreover, the conditioned medium stimulates angiogenesis as the conditioned medium comprises angiogenesis factors (column 22, lines 1-15, in particular line 15) and since VEGF is produced (column 22, line 14) which induces angiogenesis during inflammation and granulation tissue formation (column 21, lines 48-50). The conditioned medium also induces cell proliferation since it comprises growth factors which are involved in cell proliferation (column 3, lines 41-43).

In order for the conditioned medium to be used for the treatment of tissue defects, the conditioned medium must be delivered to the site of said tissue defects. Further still, the conditioned medium may be formulated with a pharmaceutically acceptable carrier (column 5,

lines 17-19) and the conditioned medium may contain collagens (column 25, lines 48-52), thus the limitations recited in instant claims 11 and 12 are disclosed.

Naughton et al. differs from the claimed invention in that it does not expressly disclose that the cell proliferation of endothelial cells is induced. However, since Naughton et al. teaches a composition comprising growth factors which are involved in cell proliferation (column 3, lines 41-43), such as vascular endothelial growth factor (column 22, line 14), cell proliferation would have been induced of a variety of cells, including endothelial cells. Moreover, it would have been obvious to have substituted the endothelial cells with any known endothelial cells, including human umbilical vein endothelial cells are recited in instant claim 19.

Naughton et al. also differs from the claimed invention in that it does not expressly disclose that the tissue culture for preparing the conditioned medium is subjected to an electromagnetic field.

Baylink discloses that "…the production of growth factor can be increased in vivo by the exogenous stimulation of living tissue with magnetic fields" (column 1, lines 53-55). Baylink teaches stimulating the production of growth factor in living tissue by the application of a magnetic field (abstract). The magnetic field may be applied with an electromagnet (column 6, lines 50-51), and thus Baylink teaches the application of electromagnetic fields for enhanced growth factor production. Baylink emphasizes that "it is to be understood that the method of the present invention is suitable for use in stimulating growth factor in a range of living tissue, including but not limited to in vitro cell cultures, animal subjects, or human subjects" (column 5, lines 28-32).

George et al. discloses the use of an electromagnetic field of specified strength and duration "…to stimulate cellular growth and proliferation,…growth factor expression,...and reductions in cell doubling time" (column 9, lines 12-17). George et al. accomplishes this by the administration of pulsed electromagnetic energy to cells (column 10, lines 4-7).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have applied an electromagnetic field, such as a pulsed electromagnetic field, to the tissue culture during incubation and prior to the extraction of the conditioned medium when performing the Naughton invention. One of ordinary skill in the art would have been motivated to do this since the application of an electromagnetic field would have increased growth factor production, thus resulting in a conditioned medium with a higher concentration of growth factors. Increased growth factor concentration is desirable since growth factors found in the conditioned media of Naughton et al. are for the treatment of tissue damage, regulate growth and differentiation, and accelerate wound healing (column 22, lines 4-26). Moreover, higher growth factor concentration is sought after by Naughton patent since it points out that the conditioned medium "…may be further processed to concentrate or reduce one or more factors or components contained within the medium. For example, the conditioned medium may be enriched with a growth factor…" (column 5, lines 23-28).

Finally, these references differ from the claimed invention in that they do not expressly disclose that the electromagnetic field applied is pulsed, or that it was applied for at least about 8 hours.

Yen-Patton et al. discloses statistically significant enhancement of growth rate of endothelial cells in the presence of pulsed electromagnetic fields (abstract). Experiments were

performed on human umbilical vein endothelial cells in the presence of a pulsed electromagnetic field, where it was found that a first nucleation site for vascularization was formed after 8 hours in the field, while after 24 hours of exposure in the field, there was tube elongation and thickening (page 42, Figure 3).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have applied a pulsed electromagnetic field for various periods of time, including administering it for at least about 8 hours. One of ordinary skill in the art would have been motivated to do this since pulsed electromagnetic field applied for at least 8 hours provides an environment suitable for endothelial cell growth. Therefore, the resulting condition medium would have been especially suitable for endothelial cell growth.

A holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments filed April 1, 2009, and June 11, 2009, have been fully considered but they are not persuasive. Guerkov is in reference to the application of a pulsed electromagnetic field on non-union cells, and does not specifically discuss endothelial cells. Therefore, it has been eliminated as a secondary reference. Yen-Patton et al. has been introduced as a new reference, which clearly teaches that pulsed electromagnetic fields stimulate the growth rate of endothelial cells, thus providing an environment supportive of tissue growth.

With respect to Baylink and George, though both references do not teach that endothelial cells are capable of producing a tissue culture medium that can be used to repair/enhance bone,

cartilage or wound tissue defects, it is respectfully noted that Naughton teaches that aspect of the claimed invention.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN E. FERNANDEZ whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Susan E. Fernandez
Examiner
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sef